PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 22 March 2001 (22.03.01)	
International application No. PCT/US00/18856	**Applicant's or agent's file reference** UCI1150WO
International filing date (day/month/year) 08 July 2000 (08.07.00)	**Priority date** (day/month/year) 08 July 1999 (08.07.99)

Applicant

FAN, Hung, Y. et al

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

01 February 2001 (01.02.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

S. Mafla

Telephone No.: (41-22) 338.83.38

US0018856

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To: LISA A. HAILE
GRAY CARY WARE & FRIEDENRICH LLP
4365 EXECUTIVE DRIVE
SUITE 1600
SAN DIEGO CA [redacted]

RECEIVED
OCT 23 2000
104695-16042 GRAYCARY/GT PATENT

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Date of Mailing *(day/month/year)* 18OCT 2000	
Applicant's or agent's file reference UCI1150WO	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/US00/18856	International filing date *(day/month/year)* 08 JULY 2000
Applicant THE REGENT OF THE UNIVERSITY OF CALIFORNIA	

1. [X] The applicant is hereby notified that the international search report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 *bis* 1 and 90 *bis* 3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer BRETT L NELSON Telephone No. (703) 308-0196

Form PCT/ISA/220 (July 1998)*

(See notes on accompanying sheet)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference UCI1150WO	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US00/18856	International filing date *(day/month/year)* 08 JULY 2000	(Earliest) Priority Date *(day/month/year)* 08 JULY 1999
Applicant THE REGENT OF THE UNIVERSITY OF CALIFORNIA		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:
   [ ] contained in the international application in written form.
   [ ] filed together with the international application in computer readable form.
   [ ] furnished subsequently to this Authority in written form.
   [ ] furnished subsequently to this Authority in computer readable form.
   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
2. [ ] **Certain claims were found unsearchable** (See Box I).
3. [X] **Unity of invention is lacking** (See Box II).
4. With regard to the **title**,
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the **drawings** to be published with the abstract is Figure No. _____
   [ ] as suggested by the applicant.
   [ ] because the applicant failed to suggest a figure.
   [ ] because this figure better characterizes the invention.
   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/18856

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C12N 1/12, 1/20
US CL : 435/235.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/235.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	YORK. D.F.et al. Isolation , identification, and partial cDNA cloning of genomic RNA of Jaagsiekte Retrovirus, the etiological agent of sheep pulmonary adenomatosis. J. Vir. September 1991. Vol. 65. No. 9. pages 5061-5067, especially abstract and pages 5061-5062.	1-3 --------- 3-24, 55-58
X ----- Y	YORK. D.F. et al. Nucleotide sequence of the Jaagskiekte Retrovirus, an exogenous and endogenous type D and B retrovirus of sheep and goats. J. Vir. August 1992. Vol. 66. No. 8. pages 4930-4939, especially abstract and pp. 4930-4931.	1-3 ---------- 4-24, 55-58
Y	US 5,849,718 A (GROSVELD) 15 December 1998, cols. 6-12.	4-16, 18-22, 24, 55-58

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 05 SEPTEMBER 2000	Date of mailing of the international search report 18 OCT 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer BRETT L. NELSON Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/18856

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,858,990 A (WALSH) 12 January 1999, cols. 15-16.	17
Y	STANDIFORD. T. J. et al Intermeukin-8 gene expression by a pulmonary epithelial cell line. J. Clin. Invest. December 1990. Vol. 86. pages 1945-1953, especially abstract.	23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/18856

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

WEST, DIALOG, MEDLINE, BIOSIS, SCISEARCH, EMBASE
search terms: Jaagsiekte sheep retrovirus, JSRV, gag, pol, env, long terminal repeats, nucleic acid, vector, cell line, host, target, suicide, marker, cancer, thymidine kinase, plasmid, cmv early promoter

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups o
f inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-3, drawn to an isolated replication competent infectious Jaagsiekte sheep retrovirus.

Group II, claim(s) 4-12, drawn to a recombinant replication competent JSRV.

Group III, claim(s) 13-24 and 55-58, drawn to an isolated JSRV genome, an isolated polynucleotide, a vector and a method of producing an infectious JRSV.

Group IV, claim(s) 25-36, drawn to a method of treating a subject having a cell proliferative disorder.

Group V, claim(s) 37-42, drawn to a pharmaceutical composition comprising a JRSV polypeptide and method of inducing an immune response.

Group VI, claim(s) 43-49, drawn to an antibody an a method of inhibiting the binding of a JRSV to a cell employing the antibody.

Group VII, claim(s) 50-53, drawn to a method for identifying a compound which binds to JRSV.

Group VIII, claim(s) 54, drawn to a method of inhibiting the expression of JRSV.

Group IX, claim(s) 59, drawn to a method of driving lung-specific expression of a heterologous polynucleotide sequence.

The inventions listed as Groups I-IX do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups I-III, V and VI recite different products which have different structures and activities and PCT rules 13.1 and 13.2 does not provide for multiple products.

Groups III-IX recite different methods which have different steps, employ different reagents and yield different results and PCT Rules 13.1 and 13.2 do not provide for multiple methods.

NOTES TO FORM PCT/ISA/220

These Notes are intended t give the basic instructions concerning the filing f amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty and of the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

The claims only.

The description and the drawings may only be amended during international preliminary examination under Chapter II.

When ? **Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).**

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? **Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.**

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confounded with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;
(ii) the claim is cancelled;
(iii) the claim is new;
(iv) the claim replaces one or more claims as filed;
(v) the claim is the result of the division of a claim as filed.

IB 14

PATENT COOPERATION TREATY

PCT

RECD 03 SEP 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UCI1150WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/18856	International filing date *(day/month/year)* 08 JULY 2000	Priority date *(day/month/year)* 08 JULY 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 1/12, 1/20 and US Cl.: 435/235.1		
Applicant THE REGENTS OF THE UNIVERSITY OF CALIFORNIA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☒ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☐ Certain observations on the international application

Date of submission of the demand 01 FEBRUARY 2001	Date of completion of this report 27 JULY 2001 29 AUG 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer STACY BROWN Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18856

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-101, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the claims:
pages 102-108, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the drawings:
pages 1-13, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18856

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 25-54,59

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 25-54,59 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18856

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- [ ] restricted the claims.
- [X] paid additional fees.
- [ ] paid additional fees under protest.
- [ ] neither restricted nor paid additional fees.

2. [ ] This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- [ ] complied with.
- [X] not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s)1-3, drawn to an isolated replication competent infectious Jaagsiekte sheep retrovirus.
Group II, claim(s) 4-12, drawn to recombinant replication competent JSRV.
Group III, claim(s) 13-24 and 55-58, drawn to an isolated JSRV genome, an isolated polynucleotide, a vector and a method of producing an infectious JSRV.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Groups I-III recite different products which have different structures and activities and PCT rules 13.1 and 13.2 do not provide for multiple products.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- [ ] all parts.
- [X] the parts relating to claims Nos. 1-24, 55-58.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18856

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	3-17,20-24,55-58	YES
	Claims	1-2,18-19	NO
Inventive Step (IS)	Claims	3,13	YES
	Claims	1-2,4-12,14-24,55-58	NO
Industrial Applicability (IA)	Claims	1-24,55-58	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-2 and 18-19 lack novelty under PCT Article 33(2) as being anticipated by York et al (1992).

Claims 1-2 are drawn to an isolated Jaagsiekte sheep retrovirus comprising gag, env and pol proteins, the corresponding genes, long-terminal repeat sequences and nucleic acid sequences necessary for other functions. Claims 1-2 are anticipated by York et al which disclose purification of JSRV containing the gag, env and pol proteins, LTRs and nucleic acid sequences encoding proteins for other functions, see page 4930, second column, first and second full paragraphs. They also disclose the nucleotide sequence of the complete genome of JSRV on page 4932, figure 3, thereby anticipating claim 18, drawn to an isolated polynucleotide comprising variant sequences and fragments of GenBank accession number AF105220. Claim 19, drawn to the corresponding RNA sequence, is disclosed on page 4930, column 2, second paragraph.

Claims 1-2, 4-12, 14-24 and 55-58 lack an inventive step under PCT Article 33(3) as being obvious over York et al (1992) in view of Grosveld.

Claims 1-2 and 18-19 are are drawn to an isolated JSRV and corresponding polynucleotide sequence and are obvious over York et al as discussed above. Claims 4-12 are drawn to a recombinant JSRV comprising gag, pol and env proteins, and a heterologous nucleic acid sequence linked to a regulatory nucleic acid sequence. The limitations of the claims include a target specific ligand (antibody, receptor or ligand) sequence on the env protein, a pulmonary cell or a cell having proliferative disorder as a target cell, a suicide gene, specifically thymidine kinase. Claims 14-16 are drawn to an isolated JSRV contained in an expression vector, such as a plasmid. Claims 20-21 are drawn to the vector having an operable association with he polynucleotide of claim 18 (anticipated by York et al, see above) and the vector transformed into a host cell. Claims 22-24 are drawn to a method for producing viral particles using the vector (Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
containing the anticipated polynucleotide of claim 18. Claims 55-58 are drawn to a recombinant retroviral vector.

York et al teach JSRV (a lentivirus) but do not teach a recombinant JSRV. Grosveld teaches a method of gene therapy, specifically, targeting specific cells with vectors. Grosveld discloses an effector system, vector, that includes a structural gene and a regulatory gene, see col.6, lines 17-21. Col.9, lines 16-19 and col.10, lines 15-17 disclose a target-specific ligand sequence present on the env protein wherein the ligand can be an antibody or ligand. Grosveld's method can be applied to cancers, see col.7, lines 29-30, which reads on claims 8-9, wherein the cell is cancerous. One of ordinary skill would have known to target a pulmonary cell (claim 7) when treating a pulmonary carcinoma. Claims 10-11 are obvious over Grosveld's teaching that the gene product (such as the well-known TK) is one that inhibits cell growth or causes cell death, see col.7, lines 19- 21. Claim 12 lacks inventive step because Grosveld discloses that the vector may comprise a selectable marker gene, see col.9, lines 31-32. Grosveld also discloses a plasmid vector comprising all sequences necessary for replication and expression, including a promoter capable of functioning in the host cell, see col.9, lines 37-47. Also taught is a vector comprising the gag, pol and env proteins, see col.9, lines 27-55.

One of ordinary skill in the art would have been motivated to substitute the JSRV disclosed by York et al into the gene targeting method of Grosveld because Grosveld et al teach a generic method of targeting specific cells affected by diseases, such as cancers, see col.7, lines 29-30. One would have incorporated the properties taught by Grosveld to maximize the effectiveness of the gene therapy vector with a reasonable expectation of success. In addition, there is motivation to combine the references in the specification of this application, see page 1, lines 28-30 and page 2, lines 8-10. Applicants disclose that it is already known in the art that there is great similarity between the disease process in ovines and humans and that the ovine disease could serve as a model for human study. One of ordinary skill would have been motivated to manufacture the ovine retrovirus in order to research therapies that give additional insight into therapies for humans with bronchiolo-alveolar carcinoma.

Claim 17 lacks an inventive step under PCT Article 33(3) as being obvious over York et al (1992) in view of Grosveld, and further in view of Walsh. Claim 17 is drawn to a JSRV wherein the regulatory sequence is a CMV early promoter sequence. York et al and Grosveld teach JSRV vector but do not teach a CMV early promoter. Walsh discloses a CMV promoter used in viral gene therapy vector, see col.15, line 59 through col.16, line 15. One of ordinary skill would have been motivated to incorporate the teaching of Walsh into the viral vector of York et al and Grosveld to improve viral vector function with a reasonable expectation of success.

Claims 3-17, 20-24 and 55-58 meet the criteria set out in PCT Article 33(2), because the prior art does not teach or fairly suggest an isolated Jaagsiekte sheep retrovirus having GenBank accession number AF105220. The prior art does not teach or fairly suggest a target sequence, a target cell, a suicide gene, a marker gene, a plasmid vector with a CMV promoter, or a method for producing a jaagsiekte sheep retrovirus.

Claims 3 and 17 meet the criteria set out in PCT Article 33(3), because the prior art does not teach or fairly suggest an isolated Jaagsiekte sheep retrovirus having GenBank accession number AF105220.

Claims 1-24 and 55-58 meet the criteria set out in PCT Article 33(4), because the claimed invention can be used in gene therapy and virus production methods.

---------- NEW CITATIONS ----------
NONE

PA NT COOPERATION TREAT

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: LISA A. HAILE
GRAY CARY WARE & FRIEDENRICH LLP
4365 EXECUTIVE DRIVE
SUITE 1600
SAN DIEGO CA 92121-2189

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)*	29 AUG 2001

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
UCI1150WO	

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/US00/18856	08 JULY 2000	08 JULY 1999

Applicant
THE REGENT OF THE UNIVERSITY OF CALIFORNIA

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	STACY BROWN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/416 (July 1992)★

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UCI1150WO	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/18856	International filing date *(day/month/year)* 08 JULY 2000	Priority date *(day/month/year)* 08 JULY 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C12N 1/12, 1/20 and US Cl.: 435/235.1		
Applicant THE REGENT OF THE UNIVERSITY OF CALIFORNIA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 01 FEBRUARY 2001	Date of completion of this report 27 JULY 2001 29 AUG 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer STACY BROWN Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18856

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-101, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the claims:
pages 102-108, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the drawings:
pages 1-13, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18856

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 25-54,59

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 25-54,59 .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18856

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- [ ] restricted the claims.
- [X] paid additional fees.
- [ ] paid additional fees under protest.
- [ ] neither restricted nor paid additional fees.

2. [ ] This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- [ ] complied with.
- [X] not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s)1-3, drawn to an isolated replication competent infectious Jaagsiekte sheep retrovirus.
Group II, claim(s) 4-12, drawn to recombinant replication competent JSRV.
Group III, claim(s) 13-24 and 55-58, drawn to an isolated JSRV genome, an isolated polynucleotide, a vector and a method of producing an infectious JSRV.

The inventions listed as Groups I-III do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Groups I-III recite different products which have different structures and activities and PCT rules 13.1 and 13.2 do not provide for multiple products.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- [ ] all parts.
- [X] the parts relating to claims Nos. 1-24, 55-58.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/18856

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	3-17,20-24,55-58	YES
	Claims	1-2,18-19	NO
Inventive Step (IS)	Claims	3,13	YES
	Claims	1-2,4-12,14-24,55-58	NO
Industrial Applicability (IA)	Claims	1-24,55-58	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-2 and 18-19 lack novelty under PCT Article 33(2) as being anticipated by York et al (1992).

Claims 1-2 are drawn to an isolated Jaagsiekte sheep retrovirus comprising gag, env and pol proteins, the corresponding genes, long-terminal repeat sequences and nucleic acid sequences necessary for other functions. Claims 1-2 are anticipated by York et al which disclose purification of JSRV containing the gag, env and pol proteins, LTRs and nucleic acid sequences encoding proteins for other functions, see page 4930, second column, first and second full paragraphs. They also disclose the nucleotide sequence of the complete genome of JSRV on page 4932, figure 3, thereby anticipating claim 18, drawn to an isolated polynucleotide comprising variant sequences and fragments of GenBank accession number AF105220. Claim 19, drawn to the corresponding RNA sequence, is disclosed on page 4930, column 2, second paragraph.

Claims 1-2, 4-12, 14-24 and 55-58 lack an inventive step under PCT Article 33(3) as being obvious over York et al (1992) in view of Grosveld.

Claims 1-2 and 18-19 are are drawn to an isolated JSRV and corresponding polynucleotide sequence and are obvious over York et al as discussed above. Claims 4-12 are drawn to a recombinant JSRV comprising gag, pol and env proteins, and a heterologous nucleic acid sequence linked to a regulatory nucleic acid sequence. The limitations of the claims include a target specific ligand (antibody, receptor or ligand) sequence on the env protein, a pulmonary cell or a cell having proliferative disorder as a target cell, a suicide gene, specifically thymidine kinase. Claims 14-16 are drawn to an isolated JSRV contained in an expression vector, such as a plasmid. Claims 20-21 are drawn to the vector having an operable association with he polynucleotide of claim 18 (anticipated by York et al, see above) and the vector transformed into a host cell. Claims 22-24 are drawn to a method for producing viral particles using the vector (Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
containing the anticipated polynucleotide of claim 18. Claims 55-58 are drawn to a recombinant retroviral vector.

York et al teach JSRV (a lentivirus) but do not teach a recombinant JSRV. Grosveld teaches a method of gene therapy, specifically, targeting specific cells with vectors. Grosveld discloses an effector system, vector, that includes a structural gene and a regulatory gene, see col.6, lines 17-21. Col.9, lines 16-19 and col.10, lines 15-17 disclose a target-specific ligand sequence present on the env protein wherein the ligand can be an antibody or ligand. Grosveld's method can be applied to cancers, see col.7, lines 29-30, which reads on claims 8-9, wherein the cell is cancerous. One of ordinary skill would have known to target a pulmonary cell (claim 7) when treating a pulmonary carcinoma. Claims 10-11 are obvious over Grosveld's teaching that the gene product (such as the well-known TK) is one that inhibits cell growth or causes cell death, see col.7, lines 19- 21. Claim 12 lacks inventive step because Grosveld discloses that the vector may comprise a selectable marker gene, see col.9, lines 31-32. Grosveld also discloses a plasmid vector comprising all sequences necessary for replication and expression, including a promoter capable of functioning in the host cell, see col.9, lines 37-47. Also taught is a vector comprising the gag, pol and env proteins, see col.9, lines 27-55.

One of ordinary skill in the art would have been motivated to substitute the JSRV disclosed by York et al into the gene targeting method of Grosveld because Grosveld et al teach a generic method of targeting specific cells affected by diseases, such as cancers, see col.7, lines 29-30. One would have incorporated the properties taught by Grosveld to maximize the effectiveness of the gene therapy vector with a reasonable expectation of success. In addition, there is motivation to combine the references in the specification of this application, see page 1, lines 28-30 and page 2, lines 8-10. Applicants disclose that it is already known in the art that there is great similarity between the disease process in ovines and humans and that the ovine disease could serve as a model for human study. One of ordinary skill would have been motivated to manufacture the ovine retrovirus in order to research therapies that give additional insight into therapies for humans with bronchiolo-alveolar carcinoma.

Claim 17 lacks an inventive step under PCT Article 33(3) as being obvious over York et al (1992) in view of Grosveld, and further in view of Walsh. Claim 17 is drawn to a JSRV wherein the regulatory sequence is a CMV early promoter sequence. York et al and Grosveld teach JSRV vector but do not teach a CMV early promoter. Walsh discloses a CMV promoter used in viral gene therapy vector, see col.15, line 59 through col.16, line 15. One of ordinary skill would have been motivated to incorporate the teaching of Walsh into the viral vector of York et al and Grosveld to improve viral vector function with a reasonable expectation of success.

Claims 3-17, 20-24 and 55-58 meet the criteria set out in PCT Article 33(2), because the prior art does not teach or fairly suggest an isolated Jaagsiekte sheep retrovirus having GenBank accession number AF105220. The prior art does not teach or fairly suggest a target sequence, a target cell, a suicide gene, a marker gene, a plasmid vector with a CMV promoter, or a method for producing a jaagsiekte sheep retrovirus.

Claims 3 and 17 meet the criteria set out in PCT Article 33(3), because the prior art does not teach or fairly suggest an isolated Jaagsiekte sheep retrovirus having GenBank accession number AF105220.

Claims 1-24 and 55-58 meet the criteria set out in PCT Article 33(4), because the claimed invention can be used in gene therapy and virus production methods.

---------- NEW CITATIONS ----------
NONE

10760

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

LISA A. HAILE
GRAY CARY WARE & FRIEDENRICH LLP
4365 EXECUTIVE DRIVE
SUITE 1600
SAN DIEGO CA 92121-2189

RECEIVED
MAR 07 2001
GRAYCARY/GT PATENT

NOTIFICATION OF RECEIPT
OF DEMAND BY COMPETENT INTERNATIONAL
PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 59.3(e) and 61.1(b), first sentence
and Administrative Instructions, Section 601(a))

Date of mailing *(day/month/year)*	27 FEB 2001
Applicant's or agent's file reference: UCI1150WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/18856	08 JUL 00	08 JUL 99

Applicant: THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

1. The applicant is hereby **notified** that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

IPEA/US 01 FEB 2001

2. That date of receipt is:

☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).

☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).

☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION**: That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

☐ *(If applicable)* This notification confirms the information given by telephone, facsimile transmission or in person on: _____

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/US Assistant Commissioner for Patents Box PCT Washington, D.C. 20231 Attn: IPEA/US Facsimile No.	Authorized officer LARRY HAMMOND Telephone No.

Form PCT/IPEA/402 (July 1998)

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

WRITTEN OPINION

(PCT Rule 66)

To: LISA A. HAILE
GRAY CARY WARE & FRIEDENRICH LLP
4365 EXECUTIVE DRIVE
SUITE 1600
SAN DIEGO CA 92121-2189

Date of Mailing *(day/month/year)*	20 APR 2001
REPLY DUE	within TWO months from the above date of mailing
Applicant's or agent's file reference: UCI1150WO	
International application No.: PCT/US00/18856	
International filing date *(day/month/year)*: 08 JULY 2000	
Priority date *(day/month/year)*: 08 JULY 1999	
International Patent Classification (IPC) or both national classification and IPC: IPC(7): C12N 1/12, 1/20 and US Cl.: 435/235.1	
Applicant: THE REGENT OF THE UNIVERSITY OF CALIFORNIA	

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I [X] Basis of the opinion
- II [ ] Priority
- III [X] Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
- IV [X] Lack of unity of invention
- V [X] Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI [ ] Certain documents cited
- VII [ ] Certain defects in the international application
- VIII [ ] Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension., see Rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 08 NOVEMBER 2001

Name and mailing address of the IPEA/US: Commissioner of Patents and Trademarks, Box PCT, Washington, D.C. 20231	Authorized officer: STACY BROWN
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

Form PCT/IPEA/408 (cover sheet) (July 1998)★

WRITTEN OPINION

International application No.
PCT/US00/18856

I. Basis of the opinion

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-109, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the claims:
pages 102-108, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the drawings:
pages 1-13, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*

WRITTEN OPINION

International application No.
PCT/US00/18856

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application.

☒ claims Nos. 25-54,59

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination *(specify)*.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _ are so unclear that no meaningful opinion could be formed *(specify)*.

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 25-54,59 .

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

WRITTEN OPINION

International application No.
PCT/US00/18856

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees the applicant has:

- [ ] restricted the claims. (See Supplemental Sheet)
- [X] paid additional fees.
- [ ] paid additional fees under protest.
- [ ] neither restricted nor paid additional fees.

2. This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1 not to invite the applicant to restrict or pay additional fees:

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

- [ ] all parts.
- [X] the parts relating to claims Nos. 1-24, 55-58.

WRITTEN OPINION

International application No.
PCT/US00/18856

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	3-17,20-24,55-58	YES
	Claims	1-2,18-19	NO
Inventive Step (IS)	Claims	3,13	YES
	Claims	1-2,4-12,14-24,55-58	NO
Industrial Applicability (IA)	Claims	1-24,55-58	YES
	Claims	NONE	NO

2. citations and explanations

Claims 1-2 and 18-19 lack novelty under PCT Article 33(2) as being anticipated by York et al (1992).

Claims 1-2 are drawn to an isolated Jaagsiekte sheep retrovirus comprising gag, env and pol proteins, the corresponding genes, long-terminal repeat sequences and nucleic acid sequences necessary for other functions. Claims 1-2 are anticipated by York et al which disclose purification of JSRV containing the gag, env and pol proteins, LTRs and nucleic acid sequences encoding proteins for other functions, see page 4930, second column, first and second full paragraphs. They also disclose the nucleotide sequence of the complete genome of JSRV on page 4932, figure 3, thereby anticipating claim 18, drawn to an isolated polynucleotide comprising variant sequences and fragments of GenBank accession number AF105220. Claim 19, drawn to the corresponding RNA sequence, is disclosed on page 4930, column 2, second paragraph.

Claims 1-2, 4-12, 14-24 and 55-58 lack an inventive step under PCT Article 33(3) as being obvious over York et al (1992) in view of Grosveld.

Claims 1-2 and 18-19 are are drawn to an isolated JSRV and corresponding polynucleotide sequence and are obvious over York et al as discussed above. Claims 4-12 are drawn to a recombinant JSRV comprising gag, pol and env proteins, and a heterologous nucleic acid sequence linked to a regulatory nucleic acid sequence. The limitations of the claims include a target specific ligand (antibody, receptor or ligand) sequence on the env protein, a pulmonary cell or a cell having proliferative disorder as a target cell, a suicide gene, specifically thymidine kinase. Claims 14-16 are drawn to an isolated JSRV contained in an expression vector, such as a plasmid. Claims 20-21 are drawn to the vector having an operable association with he polynucleotide of claim 18 (anticipated by York et al, see above) and the vector transformed into a host cell. Claims 22-24 are drawn to a method for producing viral particles using the vector (Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

IV. LACK OF UNITY OF INVENTION:

1. This response is made to a telephone Lack of Unity requirement (see telephone memorandum attached hereto or attached to a prior Written Opinion).

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
containing the anticipated polynucleotide of claim 18. Claims 55-58 are drawn to a recombinant retroviral vector.

York et al teach JSRV (a lentivirus) but do not teach a recombinant JSRV. Grosveld teaches a method of gene therapy, specifically, targeting specific cells with vectors. Grosveld discloses an effector system, vector, that includes a structural gene and a regulatory gene, see col.6, lines 17-21. Col.9, lines 16-19 and col.10, lines 15-17 disclose a target-specific ligand sequence present on the env protein wherein the ligand can be an antibody or ligand. Grosveld's method can be applied to cancers, see col.7, lines 29-30, which reads on claims 8-9, wherein the cell is cancerous. One of ordinary skill would have known to target a pulmonary cell (claim 7) when treating a pulmonary carcinoma. Claims 10-11 are obvious over Grosveld's teaching that the gene product (such as the well-known TK) is one that inhibits cell growth or causes cell death, see col.7, lines 19- 21. Claim 12 lacks inventive step because Grosveld discloses that the vector may comprise a selectable marker gene, see col.9, lines 31-32. Grosveld also discloses a plasmid vector comprising all sequences necessary for replication and expression, including a promoter capable of functioning in the host cell, see col.9, lines 37-47. Also taught is a vector comprising the gag, pol and env proteins, see col.9, lines 27-55.

One of ordinary skill in the art would have been motivated to substitute the JSRV disclosed by York et al into the gene targeting method of Grosveld because Grosveld et al teach a generic method of targeting specific cells affected by diseases, such as cancers, see col.7, lines 29-30. One would have incorporated the properties taught by Grosveld to maximize the effectiveness of the gene therapy vector with a reasonable expectation of success. In addition, there is motivation to combine the references in the specification of this application, see page 1, lines 28-30 and page 2, lines 8-10. Applicants disclose that it is already known in the art that there is great similarity between the disease process in ovines and humans and that the ovine disease could serve as a model for human study. One of ordinary skill would have been motivated to manufacture the ovine retrovirus in order to research therapies that give additional insight into therapies for humans with bronchiolo-alveolar carcinoma.

Claim 17 lacks an inventive step under PCT Article 33(3) as being obvious over York et al (1992) in view of Grosveld, and further in view of Walsh. Claim 17 is drawn to a JSRV wherein the regulatory sequence is a CMV early promoter sequence. York et al and Grosveld teach JSRV vector but do not teach a CMV early promoter. Walsh discloses a CMV promoter used in viral gene therapy vector, see col.15, line 59 through col.16, line 15. One of ordinary skill would have been motivated to incorporate the teaching of Walsh into the viral vector of York et al and Grosveld to improve viral vector function with a reasonable expectation of success.

Claims 3-17, 20-24 and 55-58 meet the criteria set out in PCT Article 33(2), because the prior art does not teach or fairly suggest an isolated Jaagsiekte sheep retrovirus having GenBank accession number AF105220. The prior art does not teach or fairly suggest a target sequence, a target cell, a suicide gene, a marker gene, a plasmid vector with a CMV promoter, or a method for producing a jaagsiekte sheep retrovirus.

Claims 3 and 17 meet the criteria set out in PCT Article 33(3), because the prior art does not teach or fairly suggest an isolated Jaagsiekte sheep retrovirus having GenBank accession number AF105220.

Claims 1-24 and 55-58 meet the criteria set out in PCT Article 33(4), because the claimed invention can be used in gene therapy and virus production methods.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

---------- NEW CITATIONS ----------
NONE

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* UCI1150WO

Box No. I TITLE OF INVENTION

A LUNG CANCER ASSOCIATED RETROVIRUS, GENE DELIVERY VECTOR AND METHODS OF USE THEREOF

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA
300 Lakeside Drive, 22nd Floor
Oakland, California 94512-3550
United States of America

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State *(that is, country)* of nationality: US

State *(that is, country)* of residence: US

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

FAN, Hung Y.
1079 Van Dyke Drive
Laguna Beach, California 92651
United States of America

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: US

State *(that is, country)* of residence: US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

Gray Cary Ware & Friedenrich LLP
4365 Executive Drive, Suite 1600
San Diego, California 92121-2189
United States of America

Telephone No. (858) 677-1456

Facsimile No. (858) 677-1465

Teleprinter No.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation f B x No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

PALMARINI, Massimo
2012 Los Trancos Dr., Apt. A ← 2019
Irvine, California 92612
United States of America

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: IT

State *(that is, country)* of residence: US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

---

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SHARP, James M.
Pentlands Science Park
Penicuik, Midlothian EH26 0PZ
United Kingdom

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: GB

State *(that is, country)* of residence: GB

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

---

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

---

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

---

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No.V DESIGNATION OF ST[redacted]

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked):*

Regional Patent

☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT

☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian

☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line):*

☒ AE United Arab Emirates
☒ AL Albania .....
☒ AM Armenia .....
☒ AT Austria .....
☒ AU Australia .....
☒ AZ Azerbaijan
☒ BA Bosnia and Herzegovina .....
☒ BB Barbados
☒ BG Bulgaria .....
☒ BR Brazil .....
☒ BY Belarus .....
☒ CA Canada
☒ CH and LI Switzerland and Liechtenstein
☒ CN China .....
☒ CR Costa Rica .....
☒ CU Cuba .....
☒ CZ Czech Republic .....
☒ DE Germany .....
☒ DK Denmark .....
☒ DM Dominica
☒ EE Estonia .....
☒ ES Spain .....
☒ FI Finland .....
☒ GB United Kingdom
☒ GD Grenada
☒ GE Georgia .....
☒ GH Ghana .....
☒ GM Gambia
☒ HR Croatia .....
☒ HU Hungary .....
☒ ID Indonesia
☒ IL Israel .....
☒ IN India .....
☒ IS Iceland
☒ JP Japan .....
☒ KE Kenya .....
☒ KG Kyrgyzstan .....
☒ KP Democratic People's Republic of Korea .....
☒ KR Republic of Korea .....
☒ KZ Kazakhstan .....
☒ LC Saint Lucia
☒ LK Sri Lanka
☒ LR Liberia
☒ LS Lesotho .....
☒ LT Lithuania
☒ LU Luxembourg
☒ LV Latvia
☒ MA Morocco .....
☒ MD Republic of Moldova .....
☒ MG Madagascar .....
☒ MK The former Yugoslav Republic of Macedonia .....
☒ MN Mongolia
☒ MW Malawi .....
☒ MX Mexico .....
☒ NO Norway
☒ NZ New Zealand .....
☒ PL Poland .....
☒ PT Portugal .....
☒ RO Romania
☒ RU Russian Federation .....
☒ SD Sudan
☒ SE Sweden
☒ SG Singapore
☒ SI Slovenia .....
☒ SK Slovakia .....
☒ SL Sierra Leone .....
☒ TJ Tajikistan .....
☒ TM Turkmenistan .....
☒ TR Turkey .....
☒ TT Trinidad and Tobago .....
☒ TZ United Republic of Tanzania
☒ UA Ukraine .....
☒ UG Uganda .....
☒ US United States of America Continuation-in-Part.....
☒ UZ Uzbekistan .....
☒ VN Viet Nam .....
☒ YU Yugoslavia .....
☒ ZA South Africa .....
☒ ZW Zimbabwe .....

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

☒ AG Antigua and Barbuda; BZ Belize .....
☒ DZ Algeria; MZ Mozambique.....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time*

Supplemental Box *If the Supplemental Box is not used, this sheet need not be included in the request.*

*1. If, in any of the Boxes, **the space is insufficient** to furnish all the information: in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:*

*(i) **if more than two persons are involved as applicants and/or inventors** and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;*

*(ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication **"the States indicated in the Supplemental Box"** is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;*

*(iii) if, in Box No. II or in any of the sub-boxes of Box No. III, **the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America:** in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;*

*(iv) if, in addition to the agent(s) indicated in Box IV, there are **further agents**: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;*

*(v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication **"patent of addition,"** or **"certificate of addition,"** or if, in Box No. V, the name of the United States of America is accompanied by an indication **"continuation"** or **"continuation-in-part"**: in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI) , the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;*

*(vi) if, in Box No. VI, there are **more than three earlier applications whose priority is claimed**: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;*

*(vii) if, in Box No. VI, **the earlier application is an ARIPO application**: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed.*

*2. If, with regard to the **precautionary designation statement** contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.*

*3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning **non-prejudicial disclosures or exceptions to lack of novelty**: in such case, write "Statement concerning non-prejudical disclosures or exceptions to lack of novelty" and furnish that statement below.*

Continuation of Box No. V: This application is a Continuation-in-Part of U.S. Provisional application no. 60/142,868 filed on 08 July 1999 (08.07.99).

Box No. VI PRIORITY CLAIM ☐ Further priority claims indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 08 July 1999 (08.07.99)	60/142,868	US		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1)

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):*

ISA/US

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*

Date *(day/month/year)* Number Country (or regional Office)

Box No. VIII CHECK LIST: LANGUAGE OF FILING

This international application contains the following **number of sheets:**

request	:	5
description (excluding sequence listing part)	:	101
claims	:	7
abstract	:	1
drawings	:	
sequence listing part of description	:	
Total number of sheets	:	114

This international application is **accompanied** by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☒ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other *(specify):* Transmittal; Postcard; Check

Figure of the drawings which should accompany the abstract: Fig.

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

The Regents of the University of California, et al.

Lisa A. Haile

Lisa A. Haile
Attorney for Applicants

For receiving Office use only

1. Date of actual receipt of the purported international application:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA/
6. ☐ Transmittal of search copy delayed until search fee is paid.

2. Drawings:
☐ received:
☐ not received:

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

This sheet is not part of [redacted] does not count as a sheet of the international application.

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference: **UCI1150WO**

Applicant: **The Regents of the University of California**

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . **240.00** T

2. SEARCH FEE . . . . . **700.00** S

International search to be carried out by **US**

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains **125** sheets.

first 30 sheets **427.00** b1

95 remaining sheets x **$10.00** additional amount = **950.00** b2

Add amounts entered at b1 and b2 and enter total at B . . **1,377.00** B

Designation Fees

The international application contains **110** designations.

8 number of designation fees payable *(maximum 8)* x **92.00** amount of designation fee = **736.00** D

Add amounts entered at B and D and enter total at I . . . . . **2,113.00** I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the

4. FEE FOR PRIORITY DOCUMENT *(if applicable)* . . . . . **15.00** P

5. TOTAL FEES PAYABLE . . . . . **3,068.00** TOTAL

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

- ☒ authorization to charge deposit account (see below)
- ☐ bank draft
- ☐ coupons
- ☒ cheque
- ☐ cash
- ☐ other *(specify)*:
- ☐ postal money order
- ☐ revenue stamps

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/ **US**

- ☐ is hereby authorized to charge the total fees indicated above to my deposit account.
- ☒ *(this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.
- ☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

50-1355 Deposit Account No.

10 July 2000 Date *(day/month/year)*

Lisa A. Haile Signature

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/18856

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 1/12, 1/20
US CL : 435/235.1

According to Internati nal Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/235.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	YORK. D.F.et al. Isolation , identification, and partial cDNA cloning of genomic RNA of Jaagsiekte Retrovirus, the etiological agent of sheep pulmonary adenomatosis. J. Vir. September 1991. Vol. 65. No. 9. pages 5061-5067, especially abstract and pages 5061-5062.	1-3 --------- 3-24, 55-58
X ----- Y	YORK. D.F. et al. Nucleotide sequence of the Jaagskiekte Retrovirus, an exogenous and endogenous type D and B retrovirus of sheep and goats. J. Vir. August 1992. Vol. 66. No. 8. pages 4930-4939, especially abstract and pp. 4930-4931.	1-3 ---------- 4-24, 55-58
Y	US 5,849,718 A (GROSVELD) 15 December 1998, cols. 6-12.	4-16, 18-22, 24, 55-58

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date f the actual completi n f the international search 05 SEPTEMBER 2000	Date of mailing of the international search report 18 OCT 2000
Name and mailing address f the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer BRETT L NELSON Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/18856

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,858,990 A (WALSH) 12 January 1999, cols. 15-16.	17
Y	STANDIFORD. T. J. et al Intermeukin-8 gene expression by a pulmonary epithelial cell line. J. Clin. Invest. December 1990. Vol. 86. pages 1945-1953, especially abstract.	23

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

WEST, DIALOG, MEDLINE, BIOSIS, SCISEARCH, EMBASE
search terms: Jaagsiekte sheep retrovirus, JSRV, gag, pol, env, long terminal repeats, nucleic acid, vector, cell line, host, target, suicide, marker, cancer, thymidine kinase, plasmid, cmv early promoter

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups o
f inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-3, drawn to an isolated replication competent infectious Jaagsiekte sheep retrovirus.

Group II, claim(s) 4-12, drawn to a recombinant replication competent JSRV.

Group III, claim(s) 13-24 and 55-58, drawn to an isolated JSRV genome, an isolated polynucleotide, a vector and a method of producing an infectious JRSV.

Group IV, claim(s) 25-36, drawn to a method of treating a subject having a cell proliferative disorder.

Group V, claim(s) 37-42, drawn to a pharmaceutical composition comprising a JRSV polypeptide and method of inducing an immune response.

Group VI, claim(s) 43-49, drawn to an antibody an a method of inhibiting the binding of a JRSV to a cell employing the antibody.

Group VII, claim(s) 50-53, drawn to a method for identifying a compound which binds to JRSV.

Group VIII, claim(s) 54, drawn to a method of inhibiting the expression of JRSV.

Group IX, claim(s) 59, drawn to a method of driving lung-specific expression of a heterologous polynucleotide sequence.

The inventions listed as Groups I-IX do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups I-III, V and VI recite different products which have different structures and activities and PCT rules 13.1 and 13.2 does not provide for multiple products.

Groups III-IX recite different methods which have different steps, employ different reagents and yield different results and PCT Rules 13.1 and 13.2 do not provide for multiple methods.